Amendments to the Claims

Please amend Claims 86 and 92. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

1. (Previously presented) A method of treating an inflamed orthopedic joint, said joint comprising i) opposing hyaline cartilage articular surfaces, ii) a peripheral collagenous capsule defining a central joint space and iii) synovial fluid contained within the joint space, comprising trans-capsularly administering into the joint space a formulation comprising an effective amount of an inhibitor of TNF-α synthesis, wherein the inhibitor of TNF-α synthesis is an anti-TNF-α monoclonal antibody or antigen-binding fragment thereof such that the inflamed orthopedic joint is treated.

2. (Original) The method of claim 1, wherein the joint is a knee joint.

3. (Withdrawn) The method of claim 1, wherein the joint is a hip joint.

4. (Withdrawn) The method of claim 1, wherein the joint is a spinal facet joint.

5. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of a pro-inflammatory interleukin.

6. (Withdrawn) The method of claim 5, wherein the interleukin is IL-1β.

7. (Withdrawn) The method of claim 5, wherein the interleukin is IL-2.

8. (Withdrawn) The method of claim 5, wherein the interleukin is IL-6.

9. (Withdrawn) The method of claim 5, wherein the interleukin is IL-8.

10. (Withdrawn) The method of claim 5, wherein the interleukin is IL-12.

11. (Withdrawn) The method of claim 5, wherein the interleukin is IL-19.

12. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of membrane-bound TNF-α.

13. (Withdrawn) The method of claim 12, wherein the high specificity antagonist is also an inhibitor of soluble TNF-α.

14. (Canceled).

15. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of a natural receptor of TNF-α.

16. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of p38 kinase selected from the group consisting of:

a) diaryl imidizole;
b) N,N'-diaryl urea;
c) N,N-diaryl urea;
d) benzophenone;
e) pyrazole ketone;
f) indole amide;
g) diamides;
h) quinazoline;
i) pyrimido [4,5-d]pyrimidinone; and
j) pyridylamino-quinazoline.

17. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of p38 kinase that is substantially water insoluble.

18. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is a 1-aryl-2-pyridinyl heterocycle is selected from the group consisting of:

a) 4,5 substituted imidazole;
b) 1,4,5 substitutued imidizole;
c) 2,4,5 substututued imidizole;
d) 1,2,4,5 substituted imidizole; and

e) non-imidizole 5-membered ring heterocycle.

19. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of NO synthase.

20. (Withdrawn) The method of claim 19, wherein the high specificity antagonist is L-NIL.

21. (Withdrawn) The method of claim 19, wherein the high specificity antagonist is N^G – monomethyl-L-arginine.

22. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an inhibitor of PLA_2.

23. (Withdrawn) The method of claim 1, wherein the antagonist is an anti-proliferative agent.

24. (Withdrawn) The method of claim 23, wherein the anti-proliferative agent comprises rapamycin.

25. (Withdrawn) The method of claim 23, wherein the anti-proliferative agent comprises a cdk inhibitor.

26. (Withdrawn) The method of claim 23, wherein the anti-proliferative agent comprises a statin.

27. (Withdrawn) The method of claim 23, wherein the anti-proliferative agent comprises an anti-oxidant.

28. (Withdrawn) The method of claim 27, wherein the anti-oxidant comprises a super oxide dismutase.

29. (Withdrawn) The method of claim 1, wherein the high specificity antagonist comprises an inhibitor of an MMP.

30. (Withdrawn) The method of claim 1, wherein the joint is a sacro-iliac joint.

31. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an apoptosis inhibitor and is selected from the group consisting of EPO mimetic peptide and an EPO mimetibody.

32. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is an apoptosis inhibitor and is selected from the group consisting of IGF-I and IGF-II.

33. (Withdrawn) The method of claim 1, wherein the high specificity antagonist is a caspase inhibitor.

34. (Previously Presented) The method of claim 1, wherein the formulation further comprises at least one growth factor.

35. (Withdrawn) The method of claim 34, wherein the additional therapeutic agent comprises glycosaminoglycans.

36. (Original) The method of claim 1, wherein the formulation further comprises a liposomal delivery system.

37. (Original) The method of claim 1, wherein the formulation is administered in an amount of less than 1 cc.

38. (Previously Presented) The method of claim 1, wherein the inhibitor of TNF-α synthesis is present in the formulation in an amount of at least 100 mg/ml.

39. (Original) The method of claim 1, wherein the formulation further comprises a sustained release device.

40. (Original) The method of claim 39, wherein the sustained release device comprises a hydrogel.

41. (Original) The method of claim 39, wherein the sustained release device provides controlled release.

42. (Original) The method of claim 39, wherein the sustained release device provides continuous release.

43. (Original) The method of claim 39, wherein the sustained release device provides intermittent release.

44. (Canceled).

45. (Original) The method of claim 39, wherein the sustained release device comprises microspheres having a plurality of degradation rates.

46. (Previously presented) The method of claim 39, wherein the sustained release device maintains the administered inhibitor of TNF-α synthesis at a therapeutically effective level.

47. (Original) The method of claim 1, wherein the formulation is provided closely adjacent to the outer wall of the capsule.

48. (Previously Presented) The method of claim 1, wherein the inhibitor of TNF-α synthesis is present in the formulation in a maximum amount of 0.5 mg.

49. (Canceled).

50. (Previously presented) The method of claim 1, wherein the formulation further comprises a growth factor is provided by platelet concentrate.

51. (Previously Presented) The method of claim 1, wherein the inhibitor of TNF-α synthesis therapeutically inhibits the production of a cytokine.

52. (Withdrawn) The method of claim 1, wherein the formulation further comprises viable mesenchymal stem cells.

53. (Original) The method of claim 1, wherein the formulation is injected into the synovial fluid.

54. (Original) The method of claim 1, wherein the formulation includes a viscosupplement.

55. (Previously Presented) The method of claim 1, wherein a portion of the synovial fluid is removed prior to administration of the inhibitor of TNF-α synthesis.

56. (Original) The method of claim 1, wherein the administration is performed through a needle.

57. (Original) The method of claim 1, wherein the formulation is administered through a drug pump.

58. (Original) The method of claim 1, wherein the formulation is administered in a volume of between 0.03 ml and 0.3 ml.

59. (Canceled).

60. (Original) The method of claim 1, wherein the administration comprises providing the formulation in a patch attached to an outer wall of the capsule.

61. (Original) The method of claim 1, wherein the administration comprises providing the formulation in a depot at a location closely adjacent an outer wall of the capsule.

62. (Original) The method of claim 1, wherein the administration comprises providing the formulation in a depot at a location closely adjacent to an endplate of an adjacent bony body.

63. (Previously Presented) The method of claim 1, wherein the inhibitor of TNF-α synthesis is predominantly released from the formulation by diffusion of the high specificity antagonist through a sustained delivery device.

64. (Original) The method of claim 63, wherein the sustained delivery device is a polymer.

65. (Previously Presented) The method of claim 1, wherein the inhibitor of TNF-α synthesis is predominantly released from the formulation by biodegradation of a sustained delivery device.

66. (Withdrawn) A method of therapeutically treating a degenerating joint, comprising:

a) determining a level of a pro-inflammatory protein within the joint,

b) comparing the level against a pre-determined level of the pro-inflammatory protein, and

c) injecting an antagonist of the pro-inflammatory protein into the joint.

67. (Withdrawn) The method of claim 66, wherein the proinflammatory protein is an interleukin.

68. (Withdrawn) The method of claim 67, wherein the predetermined level for the interleukin is at least 100 pg/ml.

69. (Withdrawn) The method of claim 66, wherein the proinflammatory protein is an interleukin-6.

70. (Withdrawn) The method of claim 69, wherein the predetermined level for the interleukin-6 is at least 100 pg/ml.

71. (Withdrawn) The method of claim 69, wherein the predetermined level for the interleukin-6 is at least 250 pg/ml.

72. (Withdrawn) The method of claim 66, wherein the proinflammatory protein is an interleukin-8.

73. (Withdrawn) The method of claim 72, wherein the predetermined level for the interleukin-8 is at least 500 pg/ml.

74. (Withdrawn) The method of claim 66, wherein the proinflammatory protein is PGE2.

75. (Withdrawn) The method of claim 74, wherein the predetermined level for PGE2 is at least 1000 pg/ml.

76. (Withdrawn) The method of claim 66, wherein the proinflammatory protein is TNF-α.

77. (Withdrawn) The method of claim 76, wherein the predetermined level for TNF-α is at least 20 pg/ml.

78. (Withdrawn) The method of claim 76, wherein the predetermined level for TNF-α is at least 30 pg/ml.

79. (Withdrawn) The method of claim 66, wherein the predetermined level for TNF-α is at least 1000 pg/joint.

80.-83. (Canceled).

84. (Withdrawn) A method of treating an inflamed orthopedic joint, wherein inflammation of the orthopedic joint results in ankylosing spondylitis, said joint comprising i) opposing hyaline cartilage articular surfaces, ii) a peripheral collagenous capsule defining a central joint space and iii) synovial fluid contained within the joint space, comprising trans-capsularly administering into the joint space a formulation comprising an effective amount of an inhibitor of TNF-α synthesis such that an inflamed joint is treated.

85. (Withdrawn) The method of Claim 84, wherein said inhibitor of TNF-α synthesis is infliximab.

86. (Withdrawn-currently amended) The method of Claim 84, wherein said inhibitor of TNF-α synthesis is ~~adalimulab~~ adalimumab.

87. (Withdrawn) The method of Claim 84, wherein said inhibitor of TNF-α synthesis is CDP-571.

88. (Withdrawn) The method of Claim 84, wherein said inhibitor of TNF-α synthesis is CDP-870.

89. (Canceled).

90. (Canceled).

91. (Previously presented) The method of claim 1, wherein the formulation further comprises BMP-1, BMP-3, BMP-2, OP-1, BMP-2A, BMP-2B, or BMP-7.

92. (Currently amended) The method of Claim 1, wherein the formulation further comprises ~~TGF-B~~ TGF-β.

93. (Previously presented) The method of Claim 1, wherein said inhibitor of TNF-α synthesis is adalimumab.

94. (Previously presented) The method of Claim 1, wherein said inhibitor of TNF-α synthesis is CDP-571.

95. (Previously presented) The method of Claim 1, wherein said inhibitor of TNF-α synthesis is CDP-870.

96. (Previously presented) A method of treating an inflamed orthopedic joint, said joint comprising i) opposing hyaline cartilage articular surfaces, ii) a peripheral collagenous capsule defining a central joint space and iii) synovial fluid contained within the joint space, comprising trans-capsularly administering into the joint space a formulation comprising an effective amount of an inhibitor of TNF-α synthesis, wherein the inhibitor of TNF-α synthesis is infliximab, such that the inflamed orthopedic joint is treated.